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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,616	11/15/2005	Roy Curtiss III	56029-51044	4042

70119 7590 06/01/2009

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
06/01/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPDOCKET@THOMPSONCOBURN.COM

Office Action Summary	Application No.	Applicant(s)	
	10/511,616	CURTISS, ROY	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,14-17,19 and 21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6,8-12,14-17,19 and 21-40* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

I. This Office is responsive to Applicant's amendment and response filed 2-9-09. Claims 1-17, 19 and 21-40 are pending. Claims 18 and 20 are cancelled.

After careful review of the record, the restriction on 9/15/2008 has been vacated in favor of the restriction requirement set forth below.

Election/Restrictions

II. Restriction is required under 35 U.S.C. 121 and 372.

III. This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

1. Group I, claims 1, and 8-10, drawn to a live attenuated derivative of a pathogenic *Salmonella* species consisting essentially (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein non-expression of said regulatory protein *in vivo* causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate antigen ceases to be synthesized *in vivo*, exposing a second carbohydrate antigen that is conserved among Salmonella species and E. coil strains; wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against *Salmonella* species and *E. coli* strains.
2. Group II, claims 2-7 and 33, drawn to a live attenuated derivative of a pathogenic *Salmonella* species consisting essentially (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein non-expression of said regulatory protein *in vivo* causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate antigen ceases to be synthesized *in vivo*, exposing a second carbohydrate antigen

that is conserved among Salmonella species and E. coil strains; wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against *Salmonella* species and *E. coli* strains.

3. Group III, claim 11, drawn to a method for inducing an immune response sufficient for protection against infection by Salmonella species and E. coil strains, said method comprising administering to an individual a live attenuated derivative of a pathogenic *Salmonella* species consisting essentially (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein non-expression of said regulatory protein *in vivo* causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate antigen ceases to be synthesized *in vivo*, exposing a second carbohydrate antigen that is conserved among Salmonella species and E. coil strains; wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against *Salmonella* species and *E. coli* strains.

4. Group IV, claims 12-16, 19, 21-22 and 33, drawn to a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a fur gene, and (b) a mutation that renders a pmi gene inoperable, wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coil strains, wherein the fur promoter is replaced with a regulatable promoter operably linked to said fur gene, a vaccine comprising a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a mutation that renders a pmi gene non functional; and (b) a regulatable promoter operably linked to said fur gene, (a) a mutation in a pmi gene that renders said pmi gene non functional; and; (b) a genetic construction that allows for regulatable expresses ion of a fur gene, wherein said fur gene is expressed when said attenuated strain is in the intestinal tract of an individual and said fur gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual.

5. Group V claims 23-25, drawn to a live attenuated derivative of a Salmonella species consisting essentially of (a) a means for regulatable synthesis of LPS O-antigen side chains, wherein said O-antigen side chains are synthesized when said attenuated derivative is in the

intestinal tract of an individual and are not synthesized when said attenuated derivative is within internal tissues of an individual; and (b) a means for regulatable expression of a fur gene, wherein said fur gene is expressed when said attenuated derivative is in the intestinal tract of an individual and wherein said fur gene is not expressed when said attenuated derivative within internal tissues of an individual wherein said attenuated derivative has increased ability to induce cross-protective immunity against infection by Salmonella species and E. coli strains.

6. Group VI: claims 27-32, drawn to a recombinant bacterial strain consisting essentially of (a) a means for regulatable expression of a virulence gene wherein said gene of (a) is a virulence gene and wherein said regulatable expression of said virulence gene renders said bacterial strain attenuated while maintaining immunogenicity.

7. Group VII, claims 34-37, drawn to a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coli strains, further comprising a means for biological containment.

8. Group VIII, claims 38-39 a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein

said first carbohydrate said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coli strains, wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coil strains, further comprising a mutation in a gene selected from the group consisting of sip and sop.

9. Group IX, claim 40 a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coli strains, wherein live attenuated derivative comprises the DELTA.ilvG3::TTaraCP$_{BAD}$lacI genetic construction.

10. Group X, claim 17, drawn to a method for inducing a cross protective immune response against Salmonella species, said method comprising administering to an individual the live attenuated derivative of a pathogenic Salmonella species consisting essentially of a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coli strains, further comprising a means for non-expression of a serotype-specific antigen.

11. The inventions listed as Groups I-X do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

12. The technical feature of linking the various groups is the mutation of various genes within a Salmonella species in order to get regulatable expression. Simpson et al and Curtiss et al as evidenced by Curtiss et al et al WO 1991/006317 Date May 16, 1991. Simpson et al (US Patent 6,521,441) teach furA, furB, and furC polynucleotides and polypeptides which correlate to a fur gene (see column 7 lines 40-67). Simpson et al teach vaccines of the present invention can be administered in a DNA form, wherein the DNA encodes one or more polypeptides. Simpson et al teach that a vaccine may be administered as a component of a genetically engineered organism or host cell such as Salmonella which expresses one or more polypeptides administered to an animal (see column 5 lines 40-67).

Simpson et al is relied upon as set forth supra however, Simpson et al does not teach a live attenuated derivative of a pathogenic Salmonella species consisting essentially of (a) a means for regulatable expression of a fur gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains; and (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate antigen ceases to be synthesized in vivo, exposing a second carbohydrate antigen that is conserved among Salmonella species and E. coil strains; wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coil strains, wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coli strains.

Curtiss et al (WO 2001/83785A2)l teach an attenuated Salmonella microorganism (see claim 6) comprising a regulated antigen delivery system (RADS), wherein the RADS

comprises (a) a vector comprising (1) a site for insertion of a gene encoding a desired gene product ; (2) a first origin of replication (ori) conferring vector replication using DNA polymerase III ; and (3) a second ori conferring vector replication using DNA polymerase I, wherein the second ori is operably linked to a first control sequence repressible by a first repressor; and (b) a gene encoding a first repressor operably linked to araCPBAD (see claims 1, 6 and 8). Curtiss et al (2001) teach an inactivating mutation of galE for lipopolysaccharide synthesis (see pg. 4 lines 25-28) and as evidenced by Curtiss et al (1991), the galE gene encodes UDP-galactose epimerase, which interconverts UDP-galactose with UDP-glucose, and permits cells grown on glucose to make UDP-galactose which is a precursor both for the LPS core and the O-antigen side chain in Salmonella (see Curtiss et al (1991) pg. 20 lines 1-20).

Furthermore, the inactivating mutation of a galE gene for lipopolysaccharide synthesis as taught by Curtiss et al (2001) as set forth supra correlates to (b) a means for regulatable synthesis of a first carbohydrate antigen, wherein said first carbohydrate antigen ceases to be synthesized in vivo, exposing a second carbohydrate antigen that is conserved among Salmonella species and E. coil strains; wherein said attenuated derivative has enhanced ability to induce cross-protective immunity against Salmonella species and E. coil strains.

It would have been prima facie obvious to one of skill in the art to insert the fur gene as taught by Simpson et al into the vector and operably linked to a regulatable promoter as taught by Curtiss et al inorder to take advantage of the regulated antigen delivery system in a live bacterial vaccine that is capable of the RADS Salmonella species to be grown in vitro under low copy number control, and after vertebrate inoculation to cause an increase in antigen production in vivo; capable of causing an effective exposure of the immunized vertebrate's lymphoid tissues to a vector encoded-foreign gene product production (see pg. 8 lines 10-20) as taught by Curtiss et al which correlates to step (a) a means for regulatable expression of a fur gene that encodes a regulatory protein, wherein a regulatable promoter is operably linked to said gene, wherein said gene is expressed when said attenuated strain is in the intestinal tract of an individual and said gene is not expressed when said gene is not expressed when said attenuated strain is within internal tissues of an individual and wherein non-expression of said regulatory protein in vivo

causes synthesis of a first antigen that is conserved among Salmonella species and E. coil strains.

Consequently, the instant invention does not make a contribution over the art. Hence there is no unity of invention.

Gene Election Requirement Applicable to Various Groups

13. In addition, each Group detailed above reads on patentably distinct gene(s). Each gene is patentably distinct because the genes are structurally unrelated, and a further restriction is applied to each various groups (see below). Applicant must further elect a gene or combination thereof, if applicable. (See MPEP 803.04).

If Group I, III is elected, applicant must further elect a combination of a regulatory protein and a carbohydrate.

If Group II is elected, applicant must further elect a combination of a regulatory protein, a carbohydrate and a serotype specific antigen.

If Group V is elected, applicant must further elect the gene involved in the synthesis of LPS O-antigens that is to be regulated.

If Group VI is elected, applicant must further elect a virulence gene that is to be regulated.

If Group VII is elected, applicant must further elect a combination of a regulatory protein and a carbohydrate and the means of biological containment,

Applicant is advised that examination will be restricted to only the elected gene or combination thereof (if applicable) and should not to be construed as a species election.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and

specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina Archie whose telephone number is 571-272-9938. The examiner can normally be reached on M-F 8:30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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